Regeneron CD20xCD3 Bispecific REGN1979 Shows Positive Results in Patients with Relapsed or Refractory B-cell Non-Hodgkin Lymphoma, including in CAR-T Failures

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93% overall response (13 of 14 patients) and 71% complete response rates (10 of 14 patients) in follicular lymphoma grades 1 to 3a treated with REGN1979 5 mg to 320 mg

57% overall response rate (4 of 7 patients) in diffuse large B-cell lymphoma (DLBCL) treated with REGN1979 80 mg to 160 mg, all of which were complete responses; these included 2 complete responses in 4 patients whose disease had progressed after CAR-T treatment

Regeneron Pharmaceuticals, Inc. (NASDAQ: **REGN**) today announced positive early-stage data for REGN1979 in patients with relapsed or refractory (R/R) B-cell non-Hodgkin lymphoma (B-NHL). The emerging data, which includes patients with R/R diffuse large B-cell lymphoma (DLBCL) who had progressed after CAR-T therapy, will be presented tomorrow at the 24thCongress of the European Hematology Association (EHA). REGN1979 is an investigational bispecific monoclonal antibody and is designed to trigger tumor killing by binding to both a B-cell tumor protein (CD20) and an immune system T-cell receptor (CD3).

"We are very encouraged by the continued high response rates observed with REGN1979 in both relapsed or refractory diffuse large B-cell lymphoma and follicular lymphoma, cancers with typically poor outcomes," said Israel Lowy, M.D., Ph.D., Senior Vice President and Head of Clinical and Translational Sciences, Oncology at Regeneron. "In this trial, two patients who failed CAR-T therapy and received REGN1979 80 mg achieved complete responses; there is currently no approved therapy for patients who progress on CAR-Ts. Our potentially registrational Phase 2 program is initiating this month and will proactively evaluate active REGN1979 doses in indolent and aggressive non-Hodgkin lymphoma."

Results from patients in the early-stage dose-escalation trial are included in the EHA presentation; these include data from fully-monitored patients as of the March 15 cut-off as well as preliminary results from additional evaluable patients. The primary objective was to assess the safety, tolerability and dose-limiting toxicities of REGN1979. Secondary objectives included an evaluation of the pharmacokinetics, immunogenicity and antitumor activity of REGN1979. In the trial, there were no dose-limiting toxicities.

As shown in the EHA presentation:

- **R/R follicular lymphoma (FL) grades 1 to 3a:** the overall response rate was 93% (13 of 14 patients) in those who received doses of 5 mg or more, with a complete response rate of 71% (10 of 14 patients).
- **R/R DLBCL:** 4 of 7 patients receiving doses of 80 mg to 160 mg achieved complete responses, with all responses ongoing.
    - In R/R DLBCL patients who had not received prior CAR-T therapy: 2 of 3 achieved a complete response.
    - In R/R DLBCL patients whose disease progressed after CD-19 directed CAR-T therapy: 2 of 4 achieved a complete response.

As of the March 2019 data cutoff, safety was evaluated in 81 patients. The most common treatment-emergent adverse events (AEs) were pyrexia (83%), cytokine release syndrome (CRS; 57%), chills (54%), infections and infestations (49%), increased C-reactive protein (38%), fatigue (38%), anemia (36%) and thrombocytopenia (30%). Six patients experienced Grade 3 or higher CRS (7%). The incidence and severity of CRS declined through optimized pre-medication, even with REGN1979 dose escalation. Grade 3 or higher AEs that occurred in at least 10% of patients were anemia (21%), lymphopenia (20%), neutropenia (17%), infections and infestations (15%), thrombocytopenia (14%) and hypophosphatemia (11%). Four patients discontinued due to AEs, which included Grade 3 hemolysis, fatigue, pneumonia and neck abscess (n=1 each). Fifty-two patients discontinued, 27 due to disease progression/recurrence, and 10 due to death. Deaths were caused by progressive disease (n=6, one with an AE of Grade 5 multi-organ failure) as well as cardiac arrest, gastric perforation, lung infection and pneumonia (n=1 each).

"REGN1979 is paving the way for a diverse and proprietary new platform of home-grown bispecific antibodies, which lack mutations or other foreign sequences and are designed to look and perform like natural human antibodies," said David M Weinreich, M.D., Senior Vice President, Head, Global Clinical Development and Co-Head, Global Development. "We currently have four different bispecific antibodies in clinical trials for both solid tumors and blood cancers and expect to add more by the end of the year. Among them is our first costimulatory bispecific antibody REGN5678, which will be investigated in combination with Libtayo in prostate cancer."

REGN1979 was granted orphan drug designation by the U.S. Food and Drug Administration (FDA) for the treatment of DLBCL in 2017 and was invented by Regeneron using the company's proprietary *VelocImmune*® technology and proprietary *Veloci-Bi*™ bispecific platform. *Veloci-Bi* allows for the generation of full-length bispecific antibodies similar to native antibodies that are amenable to production by standard antibody manufacturing techniques, and likely to have favorable antibody-like pharmaco-kinetic properties.

REGN1979 and REGN5678 are currently under clinical development for B-NHL and prostate cancer, respectively, and their safety and efficacy have not been evaluated by any regulatory authority. In addition, the potential use of REGN5678 in combination with Libtayo® (cemiplimab-rwlc) is investigational, and its safety and efficacy have not been evaluated by any regulatory authority.

Libtayo is being developed jointly by Regeneron and Sanofi under a global collaboration agreement. The generic name for Libtayo in the U.S. is cemiplimab-rwlc, with rwlc as the suffix designated in accordance with Nonproprietary Naming of Biological Products Guidance for Industry issued by the FDA.

About the Phase 1 trial
Phase 1, open-label, dose-escalation trial involves 81 B-NHL patients to date (45 DLBCL, 21 FL grades 1 to 3a, 6 mantle cell lymphoma, 6 marginal zone lymphoma and 3 with other subtypes of B-NHL) who had received prior treatment with an anti-CD20 antibody. The trial has a "3 + 3" design, in which patients are enrolled into groups receiving increasing doses of REGN1979 to help determine the recommended effective dose for later stage trials. Following enrollment in their dosing group, patients initially received REGN1979 weekly for 12 weeks, followed by doses every-other-week for 12 weeks, and then are followed for a subsequent 15 months.

About DLBCL and FL
DLBCL and FL are the two most common subtypes of B-NHL with approximately 18,000 and 14,800 new cases diagnosed in the U.S. in 2019, respectively.

DLBCL is an aggressive form of B-NHL with up to 50% of patients with advanced stage disease progressing after first-line treatment (e.g., relapsing or becoming refractory to treatment). For patients with R/R DLBCL, treatment options are limited and the prognosis is poor.

FL is a slow-growing (indolent) form of B-NHL with most cases diagnosed in advanced stages. Although median survival ranges from 8 to 15 years in advanced FL, current therapeutic options are not curative, and most patients relapse within 5 years regardless of the regimen. In some cases, FL can transform into DLBCL, at which point it is often treated in the same way as DLBCL.

About Regeneron Pharmaceuticals, Inc.
Regeneron (NASDAQ: REGN) is a leading biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led for 30 years by physician-scientists, our unique ability to repeatedly and consistently translate science into medicine has led to seven FDA-approved treatments and numerous product candidates in development, all of which were homegrown in our laboratories. Our medicines and pipeline are designed to help patients with eye diseases, allergic and inflammatory diseases, cancer, cardiovascular and metabolic diseases, neuromuscular diseases, infectious diseases and rare diseases.

Regeneron is accelerating and improving the traditional drug development process through our proprietary *VelociSuite*® technologies, such as *VelocImmune*® which produces optimized fully-human antibodies, and ambitious research initiatives such as the Regeneron Genetics Center, which is conducting one of the largest genetics sequencing efforts in the world.

For additional information about the company, please visit www.regeneron.com or follow @Regeneron on Twitter.

Regeneron Forward-Looking Statements and Use of Digital Media
This press release includes forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Regeneron Pharmaceuticals, Inc. ("Regeneron" or the "Company"), and actual events or results may differ materially from these forward-looking statements. Words such as "anticipate," "expect," "intend," "plan," "believe," "seek," "estimate," variations of such words, and similar expressions are intended to identify such forward-looking statements, although not all forward-looking statements contain these identifying words. These statements concern, and these risks and uncertainties include, among others, the nature, timing, and possible success and therapeutic applications of Regeneron's products, product candidates, and research and clinical programs now underway or planned, including without limitation REGN1979 in patients with relapsed or refractory B-cell non-Hodgkin lymphoma, follicular lymphoma, diffuse large B-cell lymphoma, and other potential indications, as well as REGN5678 (costimulatory bispecific antibody being investigated in combination with Libtayo® (cemiplimab-rwlc) Injection in prostate cancer), and Regeneron's earlier-stage product candidates (such as Regeneron's other bispecific antibodies); unforeseen safety issues resulting from the administration of products and product candidates in patients, including serious complications or side effects in connection with the use of Regeneron's product candidates (such as Libtayo, REGN1979, and REGN5678 (each, as applicable, as monotherapy or in combination with other products or product candidates)) in clinical trials; the extent to which the results from the research and development programs conducted by Regeneron or its collaborators may be replicated in other studies and lead to therapeutic applications; the likelihood, timing, and scope of possible regulatory approval and commercial launch of Regeneron's late-stage product candidates and new indications for marketed products; ongoing regulatory obligations and oversight impacting Regeneron's marketed products, research and clinical programs, and business, including those relating to patient privacy; determinations by regulatory and administrative governmental authorities which may delay or restrict Regeneron's ability to continue to develop or commercialize Regeneron's products and product candidates; competing drugs and product candidates that may be superior to Regeneron's products and product candidates; uncertainty of market acceptance and commercial success of Regeneron's products and product candidates and the impact of studies (whether conducted by Regeneron or others and whether mandated or voluntary) on the commercial success of Regeneron's products and product candidates; the ability of Regeneron to manufacture and manage supply chains for multiple products and product candidates; the ability of Regeneron's collaborators, suppliers, or other third parties (as applicable) to perform manufacturing, filling, finishing, packaging, labeling, distribution, and other steps related to Regeneron's products and product candidates; the availability and extent of reimbursement of the Company's products from third-party payers, including private payer healthcare and insurance programs, health maintenance organizations, pharmacy benefit management companies, and government programs such as Medicare and Medicaid; coverage and reimbursement determinations by such payers and new policies and procedures adopted by such payers; unanticipated expenses; the costs of developing, producing, and selling products; the ability of Regeneron to meet any of its financial projections or guidance and changes to the assumptions underlying those projections or guidance; the potential for any license or collaboration agreement, including Regeneron's agreements with Sanofi, Bayer, and Teva Pharmaceutical Industries Ltd. (or their respective affiliated companies, as applicable), to be cancelled or terminated without any further product success; and risks associated with intellectual property of other parties and pending or future litigation relating thereto, including without limitation the patent litigation and other related proceedings relating to EYLEA® (aflibercept) Injection, Dupixent® (dupilumab) Injection, and Praluent® (alirocumab) Injection, the ultimate outcome of any such proceedings, and the impact any of the foregoing may have on Regeneron's business, prospects, operating results, and financial condition. A more complete description of these and other material risks can be found in Regeneron's filings with the U.S. Securities and Exchange Commission, including its Form 10-K for the fiscal year ended December 31, 2018 and its Form 10-Q for the quarterly period ended March 31, 2019. Any forward-looking statements are made based on management's current beliefs and judgment, and the reader is cautioned not to rely on any forward-looking statements made by Regeneron. Regeneron does not undertake any obligation to update publicly any forward-looking statement, including without limitation any financial projection or guidance, whether as a result of new information, future events, or otherwise.

Regeneron uses its media and investor relations website and social media outlets to publish important information about the Company, including information that may be deemed material to investors. Financial and other information about Regeneron is routinely posted and is accessible on Regeneron's media and investor relations website (http://newsroom.regeneron.com) and its Twitter feed (http://twitter.com/regeneron).

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